REMARKS

The present application is directed to modified viral particles. Prior to this Amendment and Response, Claims 1-27 were pending. In the present Amendment and Response, applicants cancelled Claims 3-27, amended Claims 1 and 2, and added new Claims 28-47. The amendments do not introduce any new matter. Upon entry of the present amendment, Claims 1-2 and 28-47 will be pending.

Interview

Applicants thank the Examiner for extending the courtesy of a telephone interview on January 19, 2005. Applicants thank the Examiner for the Interview Summary mailed on January 21, 2005.

Support for the Claim Amendments and New Claims

The following examples illustrate the support for the amendments and new claims that is found throughout the specification as originally filed. Support for the amendments to Claim 1 is found on page 20, lines 14-16. Claim 2 was amended to correct a typographical error. Support for new Claims 28-30 is found on page 13, lines 4-8. Support for new Claims 31-32 is found on page 53, lines 13-19, and pages 57-60. Support for new Claims 33-34 is found on page 20, lines 21-23. Support for new Claim 35 is found on page 22, line 3. Support for new Claims 36-39 is found on page 53, line 29, through page 53, line 6. Support for new Claim 40 is found on page 22, lines 9-21. Support for new Claims 41-46 is found in original Claims 18-19, 22-25 and 27. Support for new Claim 47 is found on page 39, lines 4-5.

Information Disclosure Statement

The Examiner states that no English translations were provided for references 98, 99 and 91 submitted with the Information Disclosure Statement filed on August 18, 2004. English translations of the references are enclosed herewith for the Examiner's consideration.

Applicants respectfully request consideration of the references in the Supplemental Information Disclosure Statement filed December 1, 2004, and a Supplemental Information Disclosure Statement submitted herewith.

Rejection of Claims under 35 U.S.C. §112, Second Paragraph

The Examiner rejects Claims 1-2 as indefinite under 35 U.S.C. §112, second paragraph. Applicants respectfully traverse the rejection.

The Examiner states the term "partially delipidated particle" is unclear. Applicants respectfully assert that the term "partially delipidated particle" is clear. One of ordinary skill in the art would know that the term "partially delipidated" means removal of at least some of the lipids from the viral particle. Furthermore, upon amendment, Claim 1 recites a partially delipidated viral particle that comprises at least one exposed epitope not usually presented to the immune system by a non-delipidated viral particle. Applicants respectfully assert that Claim 1 particularly points out and distinctly claims the subject matter that applicants regard as their invention.

The Examiner states on page 3 that the application provides a delipidated particle with exposed epitopes not usually presented to the immune system by the untreated virus, and that the viral particle proteins are structurally changed by the delipidation process on, in, or near the surface. The Examiner states on page 3 that these definitions describe the function of the particle. Applicants respectfully assert that the properties mentioned by the Examiner characterize the structure of the delipidated particle. Upon amendment, Claim 1 recites a structural feature, that is at least one exposed epitope not usually presented to the immune system.

In view of the foregoing amendments and arguments, applicants respectfully assert that they have overcome the rejection of Claims 1-2 as indefinite under 35 U.S.C. §112, second paragraph, and request its withdrawal.

Rejection of Claims under 35 U.S.C. §112, First Paragraph

The Examiner rejects Claim 2 under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The Examiner asserts that the specification lacks enablement for the claimed immunodeficiency viral particle. Applicants respectfully assert that Claim 2, as pending upon entry of the present amendment, is enabled by the application as filed.

The Examiner asserts that the claim is drawn to a vaccine against an immunodeficiency virus. Applicants respectfully bring to the Examiner's attention that Claim 2 is directed to a modified viral particle comprising at least a partially delipidated immunodeficiency viral particle, wherein the partially delipidated viral particle initiates a positive immune response in an animal or human, and incites protection against an infectious organism. Upon entry of the present amendment, Claim 2 incorporates limitations of Claim 1, which recites a viral particle that comprises at least one exposed epitope not usually presented to the immune system by a non-delipidated viral particle. Applicants respectfully assert that the specification describes the subject matter of Claim 2 in such a way as to enable one skilled in the art to make and use the invention.

The specification describes the process of delipidating SIV and HIV that results in the claimed modified viral particles. The specification describes, on pages 51-62, administering the delipidated SIV particles to experimental animals, and initiation of an immune response in the animals. The specification summarizes on page 60, last paragraph, the detectable enhancement of the immune responses in mice upon administration of the delipidated viral particles. Accordingly, the specification enables one of ordinary skill in the art to make and use the claimed invention.

The Examiner asserts that the claimed partially delipidated viral particles are not enabled because protective immunity against HIV-1 is difficult to achieve. Applicants respectfully assert that the lack of immunodeficiency vaccines does not indicate a lack of enablement for applicants' invention as claimed. Rather, it shows that the claimed

immunodeficiency viral particle compositions that initiate positive immune responses against the virus are novel and non-obvious over the compositions available in the prior art.

The Examiner cites the article by Desrosiers (*Nature Medicine*, v. 10, pp. 221-223 (2004)), teaching that natural immune responses to HIV-1 are ineffective, to support the position that the claimed, partially delipidated particles are not enabled. Applicants respectfully submit that the ineffectiveness of the natural immune responses to HIV, asserted by the Examiner, does not preclude enablement of the claimed composition. The applicants' claimed, partially delipidated viral particles are modified to improve their immunogenicity. The specification enables one of ordinary skill in the art to make the partially delipidated viral particles and administer them to animals to induce an immune response. Thus, the specification describes the claimed subject matter in such a way as to enable one skilled in the art to which it pertains to make and use the invention.

The Examiner further discusses the variability of sequences among HIV-1 isolates and difficulties in preparation of effective vaccines, particularly those prepared from the recombinant gp120 peptides. The applicants' claimed compositions are delipidated viral particles, not recombinant peptides. The difficulties in preparation of immunodeficiency vaccines asserted by the Examiner do not preclude enablement of applicants' claimed compositions. Rather, the lack of effective immunodeficiency viral compositions that incite positive immune responses shows that applicants' claimed compositions are novel and non-obvious.

On page 5, the Examiner states that the variability of sequences among HIV-1 isolates makes it impossible to construct the epitopes for neutralizing HIV. Applicants respectfully assert that, while the variability of the sequences among HIV-1 isolates makes it difficult to isolate relevant HIV epitopes, this does not preclude enablement of the applicants' claimed compositions. Applicants' partially delipidated viral particles are prepared from the viral isolates and comprise the proteins naturally occurring in the viral particles. The delipidated viral particles possess structural properties recited in Claim 1.

Isolating the epitopes is not at issue, because the proteins are already present in the viral particles, and delipidation exposes protein epitopes not usually presented to the immune system. The at least partially delipidated viral particles advantageously induce positive immune responses when administered to a human or an animal. As discussed above, the specification enables one of ordinary skill in the art to make the delipidated viral particles and administer them to animals, resulting in an improved immune response. Thus, the specification describes the claimed subject matter in such a way as to enable one skilled in the art to which it pertains to make and use the invention.

The Examiner further asserts that there are no acceptable animal models that reflect the biological pathology of HIV. The Examiner states that SIV and SHIV animal models are imperfect, and refers to the article by Feinberg and Moore (*Nature Medicine* v. 8, pp. 207-210 (2002)) for disadvantages of SIV animals models. Applicants respectfully bring to the Examiner's attention that an *in vitro* or *in vivo* model is acceptable for patentability purposes when there is a reasonable correlation with the condition; a rigorous or an invariable correlation is not required. MPEP 2164.02; *In re Brana,* 51 F.3d 1560, 1566 (Fed. Cir. 1995); *Cross v. Iizuka*, 753 F.2d 1040, 1050 (Fed. Cir. 1985). Feinberg and Moore describe SIV models as "the most important" in spite of their imperfections (see p. 207, first column, line 4). Feinberg and Moore state the models' "obvious utility," when the limitations, some of which are inherent to all animal models of human infections, are taken into account (see p. 207, second column, second paragraph). Moreover, Feinberg and Moore discuss that any such model may underestimate the potential protective efficacy of a vaccine, just as it may overestimate it (*Id.*). Furthermore, Feinberg and Moore discuss how various vaccine immunogens tested in the SIV/SHIV model "have been greeted with substantial enthusiasm" and "were associated with significantly lowered disease progression and transmission rates" (see p. 207, last paragraph, continuing to p. 208). Thus, Feinberg and Moore show that one of ordinary skill in the art considers the SIV/SHIV model as reasonably correlating with the condition.

The Examiner also asserts that promising responses in the animal model do not directly translate into success in humans. However, applicants respectfully bring to the Examiner's attention that human testing is not required to obtain a patent. *See Scott v. Finney*, 34 F.3d 1058, 1063. For assessing the enablement aspect of patentability, an animal model should be accepted as correlating to a specific condition, unless the Examiner has evidence that one skilled the in art would not accept the model as reasonably correlating with the condition. MPEP 2164.02. In view of the foregoing, applicants respectfully assert that *in vitro* immunologic testing and the SIV animal model that the applicants used to assess immunogenic properties of the partially delipidated viral particles reasonably correlate with infection by an immunodeficiency virus in an animal or a human for the purpose of assessing induction of immune responses. To support their position, applicants enclose herewith a Declaration under 37 C.F.R. §1.132 by an expert in the field of virology. Accordingly, the application as filed is enabling for the compositions recited in Claims 1-2.

The Examiner also asserts that the composition is not enabled for its claimed use. Applicants respectfully disagree. For asserting a therapeutic or a pharmacological utility, all that is required is a reasonable correlation between the activity and the asserted use. *Nelson v. Bowler,* 626 F.2d 853, 857 (CCPA 1980); MPEP 2107.02. Applicants respectfully assert that the specification discloses preparation of the claimed partially delipidated viral particles and demonstrates induction by these particles of a positive immune response in the animals tested. One of ordinary skill in the art would consider the activity disclosed in the specification as reasonably correlating with induction of an immune response to an immunodeficiency virus in an animal or a human. Thus, the composition is enabled for its claimed use.

The claimed compositions do not have to provide complete protection from the infection in order to be enabled. Many recognized vaccines, such as a chicken pox (*varicella*) vaccine, provide partial protection, yet are considered highly useful. *Varicella* vaccine is only 70-90% effective in preventing disease, yet is considered effective for use in the community. This is because the value of an immunogenic composition lies not only in its

ability to decrease the probability of contracting the infection by an individual recipient of the composition, but in its ability to lower disease transmission and prevalence in the population as a whole. Depending on the seriousness and the prevalence of the disease, even a composition with a relatively low individual protection rate can be highly useful for protection of a community from disease. Claims 1-2 recite initiating a positive immune response in an animal or human. The specification shows that claimed composition induces an immune response in experimental animals. Under current patent rules, the showing of a statistical correlation between a particular activity and a therapeutic use is not required for patentability. *Id.* Therefore, applicants assert that the specification enables the claimed composition and its claimed use.

Applicants respectfully assert that the disclosure of the present application is enabling and contains working examples commensurate in scope with the claims. The specification provides sufficient guidance to a skilled artisan to make and use the claimed invention without undue experimentation. In view of the amendments and the foregoing arguments, applicants request withdrawal of the rejection of Claim 2 under 35 U.S.C. §112, first paragraph.

Rejection of Claims under 35 U.S.C. §102(b)

The Examiner rejects Claims 1-2 under 35 U.S.C. §102(b) as anticipated by U.S. Patent No. 5,484,396 to *Naficy* (hereinafter referred to as *Naficy*). *Naficy* describes a method and device for treatment of HIV infection by removing blood from a patient and treating blood with organic solvents in a device for the purpose of killing the virus and the infected cells. The Examiner asserts that the particles in *Naficy* are delipidated and, therefore, anticipate the particles recited in Claims 1-2. Applicants respectfully assert that amendment of Claim 1 overcomes the rejection. *Naficy* fails to teach the partially delipidated particles recited in amended Claim 1. Thus, *Naficy* fails to anticipate applicants' invention as recited in Claims 1-2 and their dependent claims.

Claim 1 recites a partially delipidated viral particle that initiates a positive immune response in an animal or human and comprises at least one exposed epitope not usually presented to the immune system of the animal or the human by a non-delipidated viral particle. *Naficy* fails to teach immunogenic viral particles that comprise exposed epitopes not usually presented to the immune system by a non-delipidated viral particle.

As noted above, *Naficy* teaches a method and device for treatment of HIV infection by treating blood with organic solvents in an extracorporeal (out-of-body) device with the purpose of killing HIV virus and blood cells infected with HIV (see, for example, *Abstract*). *Naficy* teaches a method of reducing levels of HIV in patients' blood by killing the cell-free virus and stopping or substantially reducing the replication of the virus inside the infected cells (see column 7, lines 19-25). To this end, *Naficy* teaches a method of dissolving or destroying the lipid envelope, thereby destroying the glycoprotein spikes that are associated with the lipid envelope, which renders the virus unable to penetrate and infect the healthy cells (see column 7, lines 42-47). Thus, *Naficy* teaches destruction of the lipid envelope of the HIV virus and destruction of the glycoprotein spikes but fails to teach modification of the viral particles to expose at least one epitope not usually presented to the immune system by a non-delipidated viral particle. Therefore, *Naficy* fails to anticipate the composition as claimed in Claims 1 and 2 and the corresponding dependent claims.

In general, *Naficy* does not disclose exposing previously unexposed epitopes. The *Naficy* method is "particularly useful ... to treat the units of blood, plasma or blood products before releasing them for transfusion" (column 11, lines 35-37). Accordingly, the goal of Naficy is killing the virus and destroying the glycoprotein spikes associated with the viral lipid envelope, not generating immunogenic partially delipidated viral particles by exposing epitopes through partial delipidation. *Naficy* fails to teach or suggest any immunogenic properties of the partially delipidated viral particles, or their use to initiate a positive immune response, and fails to teach the composition recited in Claims 1-2.

In view of the foregoing amendments and arguments, applicants respectfully assert that *Naficy* fails to anticipate Claims 1 and 2 and their dependent claims. Applicants request that the rejection of Claims 1 and 2 under 35 U.S.C. §102(b) be withdrawn.

CONCLUSION

The foregoing is submitted as a full and complete response to the Non-Final Office Action mailed December 7, 2004.

Applicants assert that the claims are in condition for allowance and respectfully request that the application be passed to issuance. If the Examiner believes that any informalities remain in the case that may be corrected by Examiner's amendment, or that there are any other issues which can be resolved by a telephone interview, a telephone call to the undersigned agent at (404) 815-6102 or to Dr. John McDonald at (404) 745-2470 is respectfully solicited.

Respectfully submitted,

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